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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/050,121	01/18/2002	Randolph M. Howes	2514-0051-01	7866
27874	7590	12/30/2004	EXAMINER	
CALFEE, HALTER & GRISWOLD, LLP 1110 FIFTH THIRD CENTER 21 EAST STATE STREET COLUMBUS, OH 43215-4243			CHOI, FRANK I	
			ART UNIT	PAPER NUMBER
			1616	

DATE MAILED: 12/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/050,121

Applicant(s)

HOWES, RANDOLPH M.

Examiner

Frank I Choi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 and 14-46 is/are pending in the application.
- 4a) Of the above claim(s) 5,11,17-28 and 30-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,6-10,12,14-16 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-12 and 14-46 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 November 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 103

Claims 1-4, 6-10, 12, 14-16, 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Ameta et al. (Asian J. Chem. Rev., 1(2);106-124 (1990)) in view of the acknowledged prior art, Colic (US Pat. 6,544,401) and Beattie et al. (US Pat. 5,364,344).

Ameta et al. discloses that singlet oxygen can be prepared by photosensitization in which oxygen is passed into a solution containing a dye and a substrate exposed to visible or u.v. light or by the reaction between sodium hypochlorite and hydrogen peroxide in which the other products are NaCl and water (Pgs. 108, 109).

Applicant acknowledges that singlet oxygen is effective against tumor cells and cancer (Paragraph 009). Further, it is acknowledge that the photodynamic method for producing singlet oxygen has several drawbacks, including the problem of untargeted portions of the body being exposed and expense (Paragraphs 013,014,015). It is disclosed that using a peroxide-hypochlorite anion system singlet oxygen is produced which is identical to that obtained by dye-sensitized photooxidation. (Paragraph 017). It is acknowledged that singlet oxygen is the principle bacterial oxidizing agent employed by human neutrophils and monocyte phagosomes (Paragraph 019). Applicant acknowledges that singlet oxygen is a very short-lived species of oxygen (Paragraph 084).

Colic teaches that the main component of the defense mechanism of phagocytic white cells is hypochlorite ion that is combined with peroxide to enhance the reactivity of the hypochlorite and produce singlet oxygen (Column 3, lines 43-65). Colic discloses a method of preparing a solution for use in health care products similar to that produced by the body by

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preparing a solution comprising sodium hypochlorite and hydrogen peroxide and purified water (Column 4, lines 11-13, Column 5, lines 18-56). It is taught that numerous modifications of this process are obvious to persons skilled in the art (Column 5, lines 56-60).

Beattie et al. teach the use dual lumen catheters for delivering different fluids into the blood stream (See entire document).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the combination of sodium hypochlorite and hydrogen peroxide to treat tumors. However, the prior art amply suggests the same as it is known in the art to prepare solutions containing sodium hypochlorite and hydrogen peroxide for use in health care products, that sodium hypochlorite and hydrogen peroxide react to form singlet oxygen which is effective against cancer and tumor cells. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation that the combination would be effective in treating tumors. Further, one of ordinary skill in the art, knowing that singlet oxygen is a short-lived species, would be motivated to separately combine the peroxide and hypochlorite at the point of use so as to ensure that singlet oxygen is available for treatment of the cancer or tumor cell. Furthermore, one of ordinary skill in the art would expect that by use of a dual lumen catheter the peroxide and hypochlorite could be kept separate until the last possible moment thereby ensuring the maximum concentration of singlet oxygen possible. Also, one of ordinary skill in the art would expect that simultaneous or sequential administration would be effective in treating tumors. See *Ex parte Rubin*, 128 USPQ 440 (Bd. App. 1959) (obvious to reverse order of prior art process steps); See also *In re Burhans*, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie

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obvious in the absence of new or unexpected results); In re Gibson, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Examiner has duly considered Applicant's arguments but deems them unpersuasive.

As a preliminary matter, Applicant's 1.131 affidavit is insufficient to antedate Colic (US Pat. 6,544,401). Colic discloses that the mixture of hydrogen peroxide and hypochlorite which forms singlet oxygen is effective as a microbiocide (Column 3, lines 61-68, Column 4, lines 1-13). Where the only pertinent disclosure in the reference or activity is a single species of the claimed genus, the applicant can overcome the rejection directly under 37 CFR 1.131 by showing prior possession of the species disclosed in the reference or activity. In re Stempel, 113 USPQ 77 (CCPA 1957). Where the claim under rejection recites a species and the reference or activity discloses the claimed species, the rejection can be overcome under 37 CFR 1.131 directly by showing prior completion of the claimed species or indirectly by a showing of prior completion of a different species coupled with a showing that the claimed species would have been an obvious modification of the species completed by applicant. See In re Spiller, 182 USPQ 614 (CCPA 1974). The affidavit appears to show only reduction to practice of treatment of keratosis on 9/14/93 or dermal nevus on 3/15/96 by sequentially administering hydrogen peroxide and hypochlorite from separate sources. Although Applicant mentions that one could use " $^1\text{O}_2^*$ " as irrigation for wound cavities such as emphysemas or peritonitis or a wound surface and that this would have both bactericidal and tumoricidal activity and that injectable " $^1\text{O}_2^*$ " would have advantages over PDT in a note dated 3/29/92, there is no indication as to the use of peroxide and hypochlorite from separate sources. As such, the affidavit does not show

conception of a method of treatment of tumor or bacteria using separate sources of peroxide and hypochlorite and reduction to practice thereof prior to the effective filing date of Colic.

Further, 1.131 Affidavit cannot be used to overcome a reference which claims the "same" patentable invention as defined in 37 CFR 1.601(n), i.e. is anticipated or is obvious. See MPEP Section 706.02(b) [R-2]; see also *Ex parte Standish*, 10 USPQ2d 1454 (BdPatApp&Int 1988).

Colic claims a biomimetic water solution produced by a process including the steps of introducing sodium hypochlorite into purified water and subsequently adding hydrogen peroxide. Based on the prior of record set forth in the rejection herein, it is disclosed that hypochlorite and hydrogen peroxide reacts to form singlet oxygen, that singlet oxygen is a short lived species and that single oxygen is effective in treating tumors. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to modify the claims of Colic to add the hydrogen peroxide at the time of administration in view of the short life of the single oxygen species and would expect that the biomimetic so produced would be effective in treating tumors.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 231 USPQ 375 (Fed. Cir. 1986). Further, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 208 USPQ 871 (CCPA 1981).

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The mere fact that Ameta et al. and the acknowledged prior art discloses other methods of forming singlet oxygen does not appear to overcome the rejection herein, in view, of the other art which discloses the H₂O₂/hypochlorite process for formation of singlet oxygen. Applicant argues that there is no reason a person skilled in the art would choose any particular method. However, one of ordinary skill in the art would choose the H₂O₂/hypochlorite process as it is a common method of forming singlet oxygen and singlet oxygen is effective in treating tumors. See *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945) ("Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." 325 U.S. at 335, 65 USPQ at 301.). Further, Ameta et al. must be read in view of the other prior art of record disclosing the disadvantages of photodynamic therapy and use of a mixture of hydrogen peroxide and hypochlorite to form singlet oxygen.

Applicant admits that Beattie et al. provides a means for administering two solutions simultaneously, if one wanted to do so. However, Applicant argues that there is no reason why one would want to administer at least one source of peroxide and at least one source of hypochlorite. The prior art as indicated above does suggest the combination of hypochlorite and peroxide for treatment of mammals, as such, the teachings of Beattie et al. are relevant. Further, the prior art discloses that singlet oxygen is an extremely short-lived species. As such, one of ordinary skill in the art would expect that the more immediate in time the peroxide and hypochlorite are mixed to produce singlet oxygen and in distance from the point of administration to the time of and desired area of treatment the more singlet oxygen will be available to act on the tumor cell or cancer. The dual lumen catheter would permit one to have

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the site of treatment be the site of administration and the time of mixing be the time of administration and treatment, thereby maximizing the amount of singlet oxygen for treatment of the tumor cell or cancer.

With respect to Applicant's obvious to try arguments, "[a]ny judgement on obviousness is in a sense necessarily a reconstruction based on hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper." *In re McLaughlin* 170 USPQ 209, 212 (CCPA 1971). With respect Applicant's arguments as to an unexpected advantage, the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. *In re Linter*, 173 USPQ 560 (CCPA 1972); *In re Dillon*, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991). Nor has Applicant shown that the little possibility of collateral damage could not be predicted. The prior art discloses the use of a mixture of hydrogen peroxide and hypochlorite on the body without any harmful effects. Further, given that singlet oxygen is a extremely short lived species and the other reaction products are water and chloride ion, one of ordinary skill in the art would expect that damage beyond the site of administration would be minimal.

Applicant alleges that prior to Applicant's invention no one had ever simultaneously or sequentially injected peroxide and hypochlorite into a living animal and that it could not possibly been known what the actual result would be. In the first instance, since there is no requirement

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that the claimed invention be expressly disclosed in any one or all of the references, the fact that a process may have not been done before is not dispositive of the issue of obviousness. Further, obviousness does not require absolute predictability, only a reasonable expectation of success, i.e., a reasonable expectation of obtaining similar properties. See, e.g., *In re O'Farrell*, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). Herein, as indicated above, one of ordinary skill in the art would expect that using hypochlorite and peroxide to produce singlet oxygen would be effective in treating tumors. This determination was not based on "obvious to try" but on logic and sound scientific reasoning. See *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993).

Finally, Applicant refers to various references which Applicant indicates contraindicates the safety of using hypochlorite and hydrogen peroxide in the body. However, safety of a given composition is not determinative of the issue of obviousness. Whether persons of ordinary skill in the art disagree as to the safety of a product or techniques does not determine the issue of obviousness. The issue regarding obviousness is whether the differences embodied in a combination product and the result so produced would have been non-obvious to a person of ordinary skill in the art, not whether there was a controversy over whether such was safe. *Nickola v. Peterson*, 193 USPQ 443, 447 (DC EMich 1976); *In Re Jansen*, 187 USPQ 743 (CCPA 1975).

Contrary to Applicant's arguments the claims do require the combination or composition of peroxide and hypochlorite. The peroxide and hypochlorite have to react to form singlet oxygen, as such, at least at the point of administration or target site the peroxide and hypochlorite must combine or form a composition. Further, Applicant provides no evidence that no one has ever advocated administration of hypochlorite. See *In re Geisler*, 43 USPQ2d 1362 (Fed. Cir.

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1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness.").

Applicant's reliance on *In re Hedges* and *W.L. Gore & Assocs., Inc. v. Garlock, Inc.* and *In re Fine* is misplaced. In those cases, the prior art utilized to make the rejections themselves specifically taught away from the one or more aspects or components of the claimed invention, as such, it was not proper to use or combine the references to make the rejection. The American Cancer Society statements, Bleach MSDS and Schraufstatter et al. are not utilized to make the rejection herein. As such, contrary to Applicant's footnote 4 on page 12 of the remarks (11/24/2004), said references are only secondary evidence of non-obviousness which, in this case, are insufficient to overcome the rejection herein.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Claims 1-4, 6-10, 12, 14-16, 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Rosen et al. in view of the acknowledged prior art, Vincent et al., Mallams et al., and Beattie et al. (US Pat. 5,364,344).

Rosen et al. discloses that the a well described mechanism for the formation of singlet oxygen is the interaction of hypochlorite and H₂O₂, that the other reaction products are water and chloride ion and that singlet oxygen is the mechanism by which leucocytes act on tumor cells (Pgs. 4808, 4809).

Applicant acknowledges that singlet oxygen is effective against tumor cells and cancer (Paragraph 009). Further, it is acknowledge that the photodynamic method for producing singlet

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oxygen has several drawbacks, including the problem of untargeted portions of the body being exposed and expense (Paragraphs 013,014,015). It is disclosed that using a peroxide-hypochlorite anion system singlet oxygen is produced which is identical to that obtained by dye-sensitized photooxidation. (Paragraph 017). It is acknowledged that singlet oxygen is the principle bacterial oxidizing agent employed by human neutrophils and monocyte phagosomes (Paragraph 019). Applicant acknowledges that singlet oxygen is a very short-lived species of oxygen (Paragraph 084).

Vincent et al. discloses that administration sodium hypochlorite in a single dose or as an irrigant is effective against tumor (See entire document).

Mallams et al. discloses intra-arterial infusion of hydrogen peroxide in cancer patients (Pgs. 145-152).

Beattie et al. teach the use dual lumen catheters for delivering different fluids into the blood stream (See entire document).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the combination of sodium hypochlorite and hydrogen peroxide to treat tumors. However, the prior art amply suggests the same as it is known in the art to prepare solutions containing sodium hypochlorite or hydrogen peroxide for use in the treatment of tumors or cancer and that sodium hypochlorite and hydrogen peroxide react to form singlet oxygen which is effective against cancer and tumor cells. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation that the combination would be effective in treating tumors. Further, one of ordinary skill in the art, knowing that singlet oxygen is a short-lived

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species, would be motivated to separately combine the peroxide and hypochlorite at the point of use so as to ensure that singlet oxygen is available for treatment of the cancer or tumor cell.

Furthermore, one of ordinary skill in the art would expect that by use of a dual lumen catheter the peroxide and hypochlorite could be kept separate until the last possible moment thereby ensuring the maximum concentration of singlet oxygen possible. Also, one of ordinary skill in the art would expect that simultaneous or sequential administration would be effective in treating tumors. See *Ex parte Rubin*, 128 USPQ 440 (Bd. App. 1959) (obvious to reverse order of prior art-process steps); See also *In re Burhans*, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results); *In re Gibson*, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is *prima facie* obvious.).

Examiner has duly considered Applicant's arguments but deems them moot in view of the new grounds of rejection herein.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

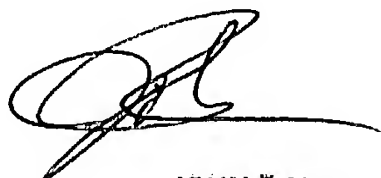
Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. Gary Kunz, can be reached at 571-272-0887. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

FIC December 26, 2004



JOHN PAK
PRIMARY EXAMINER
GROUP 1600